chromatographic profile. Until the present invention, anti-hyperglycemic effects of ginseng berry have not been reported.

The active components of *Panax ginseng* are considered to be ginsenosides, a group of steroidal saponins (Huang, 1999; Attele *et al.*, 1999). Ginsenosides are distributed in many parts of the ginseng plant, including the root, leaf and berry. The different parts of the plant contain distinct ginsenoside profiles (Huang, 1999), and these parts may have different pharmacological activities.

I. Ginsenosides

Ginseng contains over twenty ginsenosides, and single ginsenosides have been shown to produce multiple effects in the same tissue (Tsang *et al.*, 1985; Odashima et al, 1985). In addition, non-ginsenoside constituents of ginseng also exert pharmacological effects. Thus, one of skill in the art will realize that the overall activity of ginseng may potentially comprise a variety of pharmacological compounds.

A. Ginsenosides and Steroids

It is contemplated in the present invention that the active constituents may be a ginsenoside or a derivative thereof. For example, a single ginsenoside may be Re. Other examples of ginsenoside include, but are not limited to Rg1, Rb1, Rc, Rb2 or Rd. Ginsenosides (except Ro) belong to a family of steroids named steroidal saponins (Ota *et al.*, 1987; Kim *et al.*, 1998; Banthorpe, 1994). They have been named ginsenoside saponins, triterpenoid saponins, or damarene derivatives under previous classifications (Ourisson *et al.*, 1964; Boar, 1983). Ginsenosides possess the four *trans*-ring rigid steroid skeleton, with a modified side chain at C-20 (Shibata *et al.*, 1985). The classical steroid hormones have a truncated side chain (progesterone, cortisol, and aldosterone) or no side chain (estradiol and testosterone) (Banthorpe, 1994; Heftmann and Mosettig, 1960). Many steroids have a β-OH group at C-3; ginsenosides (for example, Rb1, Rb2, Rc, and Rd) usually have a sugar residue attached to the same site (Huang, 1999; Shibata *et al.*, 1985). Sugar moieties are cleaved by acid hydrolysis during extraction, or by

endogenous glycosidases to give the aglycone (Huang, 1999; Banthorpe, 1994; Shibata *et al.*, 1985).

It is also contemplated that the ginsenoside of the present invention may function mechanistically similar to steroids. Thus, one of skill in the art will realize that the mechanisms of actions that apply to steroids may also apply to ginsenosides and is within the scope of the present invention. For example, steroids possess numerous physiological activities, partly due to the nature of the steroid skeleton, which is similar to a ginsenoside. The *trans*-ring junctions of the skeleton allow substituent groups, which interact with receptors, to be held in rigid stereochemically defined orientation (Banthorpe, 1994). In addition, the steroid skeleton endows the whole molecule with a favored structure to allow, for example, insertion into membranes (Bastiaanse *et al.*, 1997). Recent work showed that Rg1 is a functional ligand of the nuclear glucocorticoid receptor (Lee *et al.*, 1997; Chung *et al.*, 1998).

B. Structural Diversity of Ginsenosides

Ginsenosides exhibit considerable structural variation. They differ from one another by the type of sugar moieties, their number, and their site of attachment. Some sugar moieties present are glucose, maltose, fructose, and saccharose. They are attached to C-3, C-6, or C-20. The binding site of the sugar has been shown to influence biological activity. Rh1 and Rh2 are structurally similar, except for the binding site of the β-d-glucopyranosyl group. In Rh1, the sugar is at C-6, and in Rh2, at C-3. Thus, it is contemplated in the present invention that the sugar moiety may be altered, *e.g.*, substitutions of sugars or changes in position of the sugar, to potentially increase the pharmacological effect. These alterations are well known in the art and are within the scope of the present invention.

In another embodiment of the present invention, the site of a hydroxyl group may be altered to increase the efficacy of the constituent or to produce a different ginsenoside. Ginsenosides also differ in their number and site of attachment of hydroxyl groups. Polar

substituents interact with phospholipid head groups in the hydrophilic domain of the membrane. Consequently, the insertional orientation of ginsenosides into membranes would be influenced by the number and site of polar OH groups. Differences in the number of OH groups were shown to influence pharmacological activity. Ginsenoside Rh2 and Rh3 differ only by the presence of an OH group at C-20 in Rh2.

Another factor that contributes to structural differences between ginsenosides is stereochemistry at C-20. Most ginsenosides that have been isolated are naturally present as enantiomeric mixtures (Banthorpe, 1994; Soldati and Sticher, 1980). Since the modules with which they react in biological systems are also optically active, stereoisomers are considered to be functionally different chemical compounds (Islam *et al.*, 1997). Consequently, they often differ considerably in potency, pharmacological activity, and pharmacokinetic profile. Both 20(S) and 20(R) ginsenoside Rg2 inhibit acetylcholine-evoked secretion of catecholamines from cultured bovine adrenal chromaffin cells (Kudo *et al.*, 1998). However, the 20(S) isomer showed a greater inhibitory effect. Thus, it is within the scope of the present invention that changes in stereochemisry may produce a different ginsenoside with a different potency. Such changes may be used to develop synthetically a constituent that has enhanced pharmacological activity that is non-naturally occurring in the berry extract.

Another embodiment of the present invention may include the use of other steroidal saponins to mimic the activity of ginsenoside. It is within in the scope of the present invention that other steroidal saponins may be modified to mimic and/or enhance the activity of the active ginsenoside constituent. It is also contemplated that these steroidal saponins or derivatives thereof may be synthetically produced for use in pharmaceutical compositions. One such example includes ganodermic acid S compounds, which are steroidal saponins that share structural features with ginsenosides (Shiao and Lin, 1987).

Also, another embodiment of the present invention includes determining the structural alterations in the ginsenosides in the gut after oral administration. It is believed